

What is claimed is:

1. A method for discrimination of p16^{INK4a} overexpressing metaplasias from p16^{INK4a} overexpressing neoplastic or preneoplastic lesions in biological samples in the course of cytological testing procedures comprising
 - 5 a. determining the presence or absence of cells overexpression of p16^{INK4a} in said biological sample;
 - b. determining the presence or absence of cells expressing at least one high risk HPV geneproduct in said biological sample;
 - 10 c. assessing simultaneous presence of cells expressing high risk HPV gene-products with cells overexpressing p16^{INK4a} or the presence of cells overexpressing p16^{INK4a} alone;
 - d. wherein the simultaneous presence of cells expressing high risk HPV gene-products with cells overexpressing p16^{INK4a} is indicative for neoplastic or preneoplastic lesion.
2. A method according to claim 1, wherein the high risk HPV gene-products are predominately expressed in early neoplastic and/or preneoplastic lesions.
3. A method according to any one of the preceding claims, wherein at least one of the HPV gene-products is encoded by the HPV E7 gene.
4. A method according to claim 1, wherein at least one of the HPV gene-products is encoded by HPV E2 and/or E6 genes.
- 20 5. A method according to claim 1, wherein at least one of the HPV gene-products is encoded by HPV L1 and/or L2 genes.
6. A method according to any one of the preceeding claims, wherein the HPV geneproduct is a polypeptide or an RNA molecule.
7. The method according to any one of the preceding claims, wherein the neoplastic or preneoplastic lesions are lesions of the anogenital tract.
- 25 8. The method according to claim 7, wherein the lesion of the anogenital tract is a lesion of the uterine cervix.
9. A method according to any preceeding claim, wherein the biological sample is a sample containing cells of anogenital origin.

10. A method according to claim 9, wherein the cells are cells originating from the uterine cervix.
11. A method according to claim 10, wherein the biological sample is a Pap-smear or a cytological preparation of the cervix uteri.
12. A method according to any one of the preceding claims, wherein the detection of the HPV gene-products and of the p16^{INK4a} molecules is performed using at least one probe specifically for the molecules to be detected.
13. A method according to claim 12, wherein the probe is detectably labelled.
14. A method according to claim 13, wherein the label is selected from the group consisting of a radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, or an enzyme.
15. A method according to any one of the claims 12 to 14, wherein the probe is a protein and/or a nucleic acid.
16. A method according to claim 15, wherein at least one probe is an antibody directed against a high risk HPV encoded geneproduct or p16^{INK4a}.
17. The method according to claim 16, which comprises an immuno-cytochemical staining procedure.
18. The method according to claim 15, wherein at least one probe is a nucleic specifically hybridizing to a high risk HPV geneproduct.
19. The method according to claim 18, which comprises an in situ hybridization reaction.
20. The method according to claim 18, which comprises a nucleic acid amplification reaction.
21. The method according to claim 20, wherein the nucleic acid amplification reaction is PCR or LCR.
22. A method according to any of the preceding claims, wherein detection reactions using nucleic acid probes and polypeptide probes are carried out simultaneously.
23. A method according to any one of the preceding claims, wherein the high risk HPV gene-products are gene-products of the cancer associated HPV subtypes HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56 and 58.
24. A method according to any of the preceding claims, wherein overexpression of p16^{INK4a} simultaneous to expression of at least one high risk HPV geneproduct in at least one single cell is determined.

25. A kit for performing the method according to any one of the preceding claims, which is a diagnostic kit or a research kit, comprising

- a. probes for the detection of the presence or absence of the overexpression of p16^{INK4a} in biological samples
- 5 b. one or more probes for the detection of the presence or absence of the expression of one or more HPV gene-products in biological samples.

26. A kit according to claim 25 furthermore comprising

- a. a p16^{INK4a} sample for carrying out a positive control reaction
- b. one or more samples of HPV gene-products for carrying out positive control reactions.